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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/272,835	03/19/99	DE SAUVAGE	F P1268R1

HM22/1027
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EXAMINER	
HAYES,R	
ART UNIT	**PAPER NUMBER**
1647	10

DATE MAILED: 10/27/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/272,835	De Sauvage et al
Examiner	**Group Art Unit**
Robert C. Hayes	1647

☒ Responsive to communication(s) filed on *Jul 20, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-15* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-15* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6 & 8*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I (Claims 1-15) in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). It is noted that all remaining claims were cancelled.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13-14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For example, the current recitation of "A host cell" encompasses a human organism. It is suggested that amending the claims to "an isolated host cell" should obviate this rejection.

3. Claims 1-15 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

While the specification asserts generic utilities for the instant invention (e.g., pages 2-3 of the specification), no known biological activity is described within the specification nor

specifically associated with any nucleic acid that encodes the polypeptides of SEQ ID NOs:15, 17 or 20, or any variants thereof. In particular, the specification merely discloses on page 55 that the human "GFRα3 does not bind any of these [GDNF family member] molecules (Figure 9C)", and that "GFRα3 is thus an orphan receptor." Therefore, the claimed polynucleotides have no specific nor substantial utility because further experimentation is necessary at the time of filing the instant invention to attribute a function and "real world" utility to the claimed nucleic acid molecules.

Applicant is directed toward the Revised Interim Utility Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification discloses on page 55 that the human "GFRα3 does not bind any of these [GDNF family member] molecules (Figure 9C)", and that "GFRα3 is thus an orphan receptor." Therefore, the actual function of the claimed encoded GFRα3 polypeptides is unknown at the time of filing the instant application; thereby, preventing the skilled artisan from knowing "how to use" the instant invention without requiring undue experimentation to first discover the function of the polynucleotides encoding the polypeptides of SEQ ID Nos: 15, 17 & 20, or variants thereof.

Additionally, the name "nucleic acid having at least 65/75% sequence identity to a nucleic acid encoding a GFRα3 polypeptide" (as it relates to how it is defined on pages 8-9 of the specification) does not sufficiently characterize and enable the polynucleotides that are encompassed by the claims, because the inclusion of any addition, substitution and deletion variants thereof, or any biologically functional equivalent encoded proteins within the definition of polynucleotides that encode such polypeptides sets forth little structural and no functional characteristics. In contrast, the specification does not teach which particular amino acids are critical for any GFRα3-related receptor protein's function that are encoded by these polynucleotides; nor how to distinguish any variants thereof (i.e., as it relates to claims 1-4, 7

& 9), or "hybridization" products thereof encompassed by the current claim limitations, from any different nucleic acid molecule that possesses none of the desired functions of the instant invention (i.e., as it especially relates to claims 8 & 10). Therefore, the skilled artisan would reasonably expect that any such random mutation to a nucleic acid encoding a putative GFRα3-related molecule with no assayable activity would result in a polynucleotide encoding an inactive protein (i.e., as it relates especially to claim 3). For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for an encoded GFRα3-related protein's function would prevent the skilled artisan from determining whether any random modification or mutation to a nucleic acid molecule that encodes a GFRα3-related protein could be made which retains the desired function of the instant invention, because any such random mutation manifested within an encoded GFRα3-related polypeptide would be predicted to adversely affect the three-dimensional conformation of the encoded polypeptide, without requiring undue experimentation to determine otherwise.

6. Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. as based on a disclosure which is not enabling.

Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. When biological material is required to practice an invention, and if it is not so obtainable or available, the enablement requirements of 35 USC §112, first paragraph, may be satisfied by a deposit of the material. See 37 CFR 1.802.

The specification lacks sufficient deposit information for the cDNAs deposited with the ATCC. Because these cDNAs are unknown, and therefore, publicly not available or can reproducibly isolated from nature without undue experimentation, a suitable deposit for patent purposes is required. See M.P.E.P. 608.01(p)(C).

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be **irrevocably removed** upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification. In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

7. Claims 8 & 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unknown what metes and bounds "stringent [hybridization] conditions" entail, because it is unknown whether low, moderate or high stringent conditions are envisioned, or what parameters defines such conditions.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-15 are rejected under 35 U.S.C. 102(a) as being anticipated by Sanicola-Nadel et al. (WO97/44356; IDS REF #6).

Sanicola-Nadel et al. disclose a polynucleotide encoding a GFRα3-related/RetL3 protein (i.e., SEQ ID NO:21, pgs. 7, 33-34 & 85-86, Fig. 10), which would hybridize under stringent conditions to nucleic acids encoding SEQ ID NOs: 15, 17 or 20, due to Sanicola-Nadel's cDNAs being 100% identical to SEQ ID NO:15/20 at the recited residue positions, or 98.7% identical to SEQ ID NO: 17 (i.e., as it relates to claims 1-2, 4-6 & 9-10, or the deposited cDNAs of claims 7-8), as well as functional variants thereof (e.g., pgs. 3, 9 & 16). In that Sanicola-Nadel disclose a polynucleotide encoding a soluble polypeptide fragment "wherein the GPI anchor sequence is absent or substituted or inactive", by definition (e.g., encoded soluble variants or SEQ ID NO:18; pgs. 7, 11, 27, 79 & 89), the limitation of claim 3 is met. In that Sanicola-Nadel's polynucleotide sequence was cloned in a λ vector, and transfected into *E.coli* host cells, in which Sanicola-Nadel's human RetL3 protein is subsequently expressed and isolated, the limitations of claims 11-15 are also met (e.g., pg. 3 & 33-34).

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
October 11, 2000

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